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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,006	MONTERO JULIAN ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *16-18* is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for monoclonal antibodies produced from hybridoma I-2068, does not reasonably provide enablement for use of other monoclonal antibodies in the method of claims 1-10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Except for the monoclonal antibodies produced from hybridoma I-2068, the specification does not teach any other monoclonal antibody that has the properties of not interfering with the fixing of IL-5 to its receptor and does not inhibit the biological activity of IL-5. Thus, the specification only provides enablement for monoclonal antibodies from hybridoma I-2068 as opposed to any other monoclonal antibodies. The claims are not limited to the monoclonal antibodies from hybridoma I-2068 and thus the scope of the claims are not enabled by the specification.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention – the invention is directed toward a process for the detection or quantification of eosinophils and basophils using an anti-IL5 monoclonal antibody which does not interfere with the fixing of IL-5 to its receptor and which does not inhibit the biological activity of IL-5.

The predictability or lack thereof of in the art – it is not predictable that any monoclonal antibody, other than those produced from hybridoma I-2068, will not interfere with the fixing of IL-5 to its receptor and does not inhibit the biological activity of IL-5.

The amount of direction or guidance present – no guidance is available to teach a skilled artisan an anti-IL5-receptor monoclonal antibody, other than those produced from hybridoma I-2068, which does not interfere with the fixing of IL-5 to its receptor and which does not inhibit the biological activity of IL-5. The instant specification fails to disclose the manner in which monoclonal antibodies are generated witht e required properties recited in the instant claim 1. The only monoclonal antibodies with the required properties are those generated from hybridoma I-2068.

The presence or absence of working examples – there is no working example in the specification of monoclonal antibodies, other than those produced from hybridoma I-2068, which does not interfere with the fixing of IL-5 to its receptor and which does not inhibit the biological activity of IL-5.

The quantity of experimentation necessary – it would be undue experimentation for a skilled artisan to make and use the inventions as claimed since not all monoclonal antibodies will not interfere with the fixing of IL-5 to its receptor and will not inhibit the biological activity of IL-5.

The relative skill of those in the art – the level of skill in the art is high.

The breadth of the claims – the claims do not limit the method to use of monoclonal antibodies from hybridoma I-2068.

In summary, the specification does not teach how a monoclonal antibody, except those from hybridoma I-2068, will not interfere with the fixing of IL-5 to its receptor and does not inhibit the biological activity of IL-5. Thus, the specification only provides enablement for monoclonal antibodies produced from hybridoma I-2068 that will not interfere with the fixing of IL-5 to its receptor and does not inhibit the biological activity of IL-5, and does not provide enablement for the other monoclonal antibodies. The instant specification lacks sufficient guidance to enable one of ordinary skill in the art to produce other monoclonal antibodies with properties required in instant claim 1. Since the claims are not limited to monoclonal antibodies produced from hybridoma I-2068, the scope of the claims are not enabled by the specification. Thus, based on the limited disclosure of the specification and the breadth of the claims, the specification is only

enabled for monoclonal antibodies from hybridoma I-2068, but not for any other monoclonal antibodies.

2. Claims 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that monoclonal antibodies from hybridoma I-2068 are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

The following sets forth the reason why monoclonal antibodies from hybridoma I-2068 are required to practice the claimed invention.

Except for monoclonal antibodies from hybridoma I-2068, the specification does not teach how a monoclonal antibody will not interfere with the fixing of IL-5 to its receptor and does not inhibit the biological activity of IL-5. Since the claims require that the monoclonal antibody not interfere with the fixing of IL-5 to its receptor and not inhibit the biological activity of IL-5, the monoclonal antibodies from hybridoma I-2068 are required to practice the claimed invention because they are the only monoclonal antibodies disclosed in the specification as having this capability. Thus, the specification only provides enablement for monoclonal antibodies from hybridoma I-2068 as opposed to any other monoclonal antibodies.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention – the invention is directed toward a process for the detection or quantification of eosinophils and basophils using an anti-IL5 monoclonal antibody which does not interfere with the fixing of IL-5 to its receptor and which does not inhibit the biological activity of IL-5.

The predictability or lack thereof of in the art – it is not predictable that any monoclonal antibody, other than those produced from hybridoma I-2068, will not

interfere with the fixing of IL-5 to its receptor and does not inhibit the biological activity of IL-5.

The amount of direction or guidance present – no guidance is available to teach a skilled artisan an anti-IL5-receptor monoclonal antibody, other than those produced from hybridoma I-2068, which does not interfere with the fixing of IL-5 to its receptor and which does not inhibit the biological activity of IL-5. The instant specification fails to disclose the manner in which monoclonal antibodies are generated witht e required properties recited in the instant claim 1. The only monoclonal antibodies with the required properties are those generated from hybridoma I-2068.

The presence or absence of working examples – there is no working example in the specification of monoclonal antibodies, other than those produced from hybridoma I-2068, which does not interfere with the fixing of IL-5 to its receptor and which does not inhibit the biological activity of IL-5.

The quantity of experimentation necessary – it would be undue experimentation for a skilled artisan to make and use the inventions as claimed since not all monoclonal antibodies will not interfere with the fixing of IL-5 to its receptor and will not inhibit the biological activity of IL-5.

The relative skill of those in the art – the level of skill in the art is high.

The breadth of the claims – the claims do not limit the method to use of monoclonal antibodies from hybridoma I-2068.

In summary, the specification does not teach how a monoclonal antibody, except for those from hybridoma I-2068, will not interfere with the fixing of IL-5 to its receptor

and does not inhibit the biological activity of IL-5. The instant specification lacks sufficient guidance to enable one of ordinary skill in the art to produce other monoclonal antibodies with properties required in the instant claims. Since the claims require that the monoclonal antibody not interfere with the fixing of IL-5 to its receptor and not inhibit the biological activity of IL-5, the monoclonal antibodies from hybridoma I-2068 are required to practice the claimed invention because it is the only monoclonal antibody disclosed in the specification as having this capability. Thus, the specification only provides enablement for monoclonal antibodies from hybridoma I-2068 that will not interfere with the fixing of IL-5 to its receptor and do not inhibit the biological activity of IL-5, and the specification does not provide enablement for any other monoclonal antibodies.

Claim Rejections - 35 USC § 112

Claims 1-10 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5-8 recite using monoclonal antibodies to other markers on the eosinophils and/or basophils in addition to the anti-IL5 monoclonal in claim 1. What is

the function of these additional monoclonal antibodies? Claims 5-8 don't say anything about what these additional monoclonals are doing in the method of claim 1.

It is unclear as to whether a label is required in claim 1. Is a label required on the anti-IL5 antibody?

Claims 9 and 10 don't seem to further limit claim 1. Claim 1 is a method for detection of eosinophils and basophils or quantifying eosinophils and basohils. Claims 9 and 10 are directed to a method of detecting or quantifying just eosinophils. Are claims 9 and 10 a separate method from claim 1?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claim 11 is rejected under 35 U.S.C. 102(e) as being anticipated by Koike et al., 6,018,032.

Koike et al. disclose an anti-IL-5R antibody (col. 1, line 66) characterized by: binding to both eosinophils and basophils (inherently); the absence of interference with

the fixing of IL-5 t its receptor (see column 1, lines 64-67; column 5, lines 8-21), the absence of interference with IgE, the absence of interference with cell activation of eosinophils or basophils, the absence of inhibition of the biological activity of IL-5 (see column 75, lines 1-5, which discloses monoclonal antibodies that bind to human IL-5 receptor alpha chain, as opposed to the monoclonal antibodies in column 75, lines 6-10, which can bind to human IL-5 receptor alpha chain and which can inhibit the biological activity of human IL-5.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koike et al., 6,018,032, in view of Monahan et al., "Attenuation of IL-5 mediated signal transduction, eosinophil survival, and inflammatory mediator", Journal of Immunology, Vol. 159(8), pp. 4024-4034, 1997.

Koike et al. discloses the invention substantially as claimed. More specifically, Koike et al. discloses that anti-IL-5R antibody can be used for the detection of eosinohils (see column 5, lines 9-18.)

However, Koike et al. does not disclose that IL-5 anti-receptor (alpha chain) monoclonal antibody can also be used to detect basophils.

Monhahan et al. however discloses that IL-5 anti-receptor (alpha chain) binds to eosinophils as well as basophils. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the Koike method of utilizing IL-5 anti-receptor (alpha chain) to detect basophils for medical research such as allergic disease research to also detect basophils because Monahan et al. teaches that IL-5 anti-receptor (alpha chain) binds to basophils as well as eosinophils.

Also, as to claim 4, the detecting step uses a flow cytometer (col. 72, line 5.)

3. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koike et al., 6,018,032, in view of Monahan et al., "Attenuation of IL-5 mediated signal transduction, eosinophil survival, and inflammatory mediator", Journal of Immunology, Vol. 159(8), pp. 4024-4034, 1997, as applied to claim 1, and further in view of Gerard et al., 6,537,764.

Koike et al. in view of Monahan et al. discloses the invention substantially as claimed (see above regarding claim 1), except for bringing into contact the sample with other monoclonal antibodies directed against other markers of the eosinophil or basophil cell types, specifically markers CD3, CD16 and CD19.

Gerard et al. teaches use of monoclonal antibodies against CD3, CD16 and CD19 to bind to basophils (col. 65, line 35 – col. 66 line 1.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to further utilize the monoclonal antibodies against CD3, CD16 and CD19, taught by Gerard et al., to detect

basophils in the method taught by Koike et al. in view of Monahan et al. because such a step provides the advantage of further verifying the presence of basophils.

4. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koike et al., 6,018,032, in view of Monahan et al., "Attenuation of IL-5 mediated signal transduction, eosinophil survival, and inflammatory mediator", Journal of Immunology, Vol. 159(8), pp. 4024-4034, 1997, as applied to claim 1, as applied to claim 1 above, and further in view of Fureder et al., "The surface membrane antigen phenotype of human blood basophils", Allergy: European Journal of Allergy and Clinical Immunology, (1994) 49/10, pp. 861-865.

Koike et al. in view of Monahan et al. discloses the invention substantially as claimed (see above regarding claim 1), except for bringing into contact the sample with other monoclonal antibodies directed against other markers of the basophil cell types, specifically marker CD63 antigen.

Fureder et al. teaches monoclonal antibodies against CD63 on basophils (see abstract. It would have been obvious to one of ordinary skill in the art at the time the invention was made to further utilize monoclonal antibodies against CD63, taught by Fureder et al., in the method taught by Koike et al. in view of Monahan et al. because such a step provides the advantage of further verifying the presence of basophils.

5. Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koike et al., 6,018,032, in view of Monahan et al., "Attenuation of IL-5 mediated signal transduction, eosinophil survival, and inflammatory mediator", Journal of Immunology, Vol. 159(8), pp. 4024-4034, 1997, as applied to claim 1, and further in view of Matsumoto et al., "CD44 and CD69 represent different types of cell-surface activation markers for human eosinophils", American journal of respiratory cell and molecular biology, 18(6), pp. 860-6, 1998.

Koike et al. in view of Monahan et al. discloses the invention substantially as claimed (see above regarding claim 1), except for bringing into contact the sample with other monoclonal antibodies directed against other eosinophil activation markers, specifically CD69 antigen.

Matsumoto et al. discloses that monoclonal antibodies directed against CD69 antigen bind to eosinophils (see abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was made to further utilize monoclonal antibodies against CD69, taught by Matsumoto et al., in the method taught by Koike et al. in view of Monahan et al. because such a step provides the advantage of further verifying the detection of eosinophils.

6. Claims 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jackson et al., 5,776,709, in view of Koike et al., 6,018,032.

Jackson et al. discloses the invention substantially as claimed. Jackson discloses a kit for the analysis of leukocytes, the kit comprising a mixture of antibody

markers for lymphocytes, monocytes and neturophils, conjugated to a second fluorochrome (see column 10, line 67 – col. 11, line 1), antibodies directed against activation markers and conjugated to a third fluorochrome (see column 11, lines 3-4.)

Jackson et al. also discloses using an antibody conjugated to a first fluorochrome (col. 10, lines 66-67.) However, Jackson et al. does not specify that the anti-leukocyte antibody is anti-IL-5R antibody. Jackson et al. however does teach that the antibodies are selected to be specific for and to bind to any antigen for detection of any cellular characteristic of interest to the investigator (col. 8, lines 12-14.) Jackson et al. additionally discloses eosinophils as a leukocyte subpopulation of clinical interest (col. 1, lines 38-39.

Koike et al. teaches antibodies, specifically, anti-IL-5R antibodies, that bind to eosinophils and thus can be used for the detection of eosinophils (see column 5, lines 9-18.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the anti-IL-5R antibody taught by Koike et al. in the Jackson method because it is for the detection of leukocytes generally disclosed by Jackson to be of clinical interest.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.L.

Christopher L. Chin

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PRIMARY EXAMINER
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1/24/05